

CLAIMS

1. A refolded recombinant T cell receptor (TCR) which comprises:
- 5 i) a recombinant TCR α or γ chain extracellular domain having a first heterologous C-terminal dimerisation peptide; and
- ii) a recombinant TCR β or δ chain extracellular domain having a second C-terminal dimerisation peptide which is specifically heterodimerised with the first dimerisation peptide to form a
- 10 heterodimerisation domain.
2. A biologically-active recombinant T cell receptor (TCR) which comprises:
- i) a recombinant TCR α or γ chain extracellular domain having a first heterologous C-terminal dimerisation peptide; and
- 15 ii) a recombinant TCR β or δ chain extracellular domain having a second C-terminal dimerisation peptide which is specifically heterodimerised with the first dimerisation peptide to form a heterodimerisation domain.
3. The recombinant TCR according to claim 1 or claim 2,
- 20 wherein a disulphide bond present in native TCRs between the α and β or γ and δ chains adjacent to the cytoplasmic domain, is absent.
4. The recombinant TCR according to claim 1, 2 or 3, wherein the heterodimerisation domain is a coiled coil domain.
5. The recombinant TCR according to claim 4, wherein the
- 25 dimerisation peptides are c-jun and c-fos dimerisation peptides.
6. The recombinant TCR according to any one of claims 1 to 5, comprising a flexible linker located between the TCR chains and the heterodimerisation peptides.
7. The recombinant TCR according to any one of claims 1 to 6,
- 30 expressed in an *E. coli* expression system.

8. The recombinant TCR according to any one of claims 1 to 7, which is biotinylated at the C-terminus.
9. The recombinant TCR according to any one of claims 1 to 8, labelled with a detectable label.
- 5 10. The recombinant TCR according to any one of claims 1 to 9, linked to a therapeutic agent such as a cytotoxic agent or an immunostimulating agent.
11. Nucleic acid sequences encoding the recombinant TCR chains of the recombinant TCR according to any one of claims 1 to 7.
- 10 12. A nucleic acid sequence according to claim 11, in an *E. coli* expression vector.
13. A method of making a recombinant non membrane bound T cell receptor, which method comprises expressing:
- 15 i) a recombinant TCR α or γ chain extracellular domain having a first heterologous C-terminal dimerisation peptide; and
- ii) a recombinant TCR β or δ chain extracellular domain having a second C-terminal dimerisation peptide which specifically heterodimerises with the first dimerisation peptide to form a heterodimerisation domain; and refolding the chains together *in vitro* to produce a TCR heterodimer.
- 20 14. The method according to claim 13, wherein refolding is carried out in a refolding buffer comprising a solubilising agent.
15. The method according to claim 14, wherein the solubilising agent is urea at a concentration of at least 0.1M.
- 25 16. The method according to claim 15, wherein the solubilising agent is urea at a concentration of about 5M.
17. The method according to any one of claims 13 to 16, wherein the chains are denatured in a denaturing buffer prior to refolding.
18. The method according to claim 17, wherein the denaturing buffer contains DTT or guanidine as a reducing agent.
- 30 19. The method according to any one of claims 13 to 18, wherein the TCR is the recombinant TCR according to any one of claims 1 to 7.

20. A recombinant TCR produced by the method according to any one of claims 13 to 19.
21. A multimer of the TCR according to claim 20.